REMARKS

Prior to the present reply, claims 1-22 and 24-39 were pending. Due to a restriction requirement, claim 31-35 are withdrawn from consideration. Claims 1-22, 24-30, and 36-39 are thus under examination. These claims are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite, under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement, and under 35 U.S.C. § 103(a) as being obvious over WO 01/04156 ("Larsen")[1] in view of Roach et al., Diabetes Care 22:1258-61, 1999 ("Roach"). These claims are also provisionally rejected on the grounds of obviousness-type double patenting over clams 1-8 of U.S. Patent Application No. 12/277,148 ("the '148 application"). Each of these rejections is addressed below.

The invention

Applicant has discovered that the therapeutic effects of GLP-1 agonists persist after administration has ceased. The exemplary GLP-1 agonist, Compound 1, was administered to diabetic mice for fifty days. Following cessation of administration, fasting glucose blood levels (Figure 5), oral glucose tolerance (Figure 6), level of pancreatic insulin mRNA (Figure 7), and glucose-bound hemoglobin (HbA_{1c}) levels (Figure 8) were all improved for at least forty days as compared to untreated animals. Based on this discovery, the claims are directed to methods of treating diabetes or a related disorder using a GLP-1 agonist, where the agonist is not continuously present.

Claim amendments

Claims 1-6, 10-15, 20-22, 28, and 39 have been amended. Claims 1-6, 10-15, and 20-22 have been amended to recite a GLP-1 agonist. Support for this amendment is found, for example, at page 10, line 6. Claim 22 has also been amended with regard to the exendin-4 analog or derivative. Support for this amendment is found, for example, at

1 The action cites PCT Publication WO **91**/04156, which the Office indicates was cited on applicant's IDS. WO **01**/04156 was cited on applicant's IDS and discloses the des Pro^{36}-exendin-4(1-39)-Lys_6-NH_2 mentioned in the action. Applicant therefore concludes the Office intended to cite WO 01/04156.

page 16, line 27, and at page 10, lines 7-9. Claim 28 has been amended to recite that the insulin analog is a recognized anti-diabetic drug. Support for this amendment is found, for example, at page 20, line 19. Claims 11 and 12 have been amended to recite that the agonist is administered *as a* bolus, and claim 39 has been amended to delete the term "diabetes associated with a genetic syndrome." No new matter has been added by the present amendment.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 1-22, 24-30, and 36-39 are rejected as being indefinite. In particular, the Office states that the terms "GLP-1 effect" recited in claim 1, "mammal bolus" recited in claims 11 and 12, and diabetes "associated" with a genetic disorder recited in claim 39 are vague and indefinite.

Without assenting to this rejection, claim 1 has been amended to recite a "GLP-1 agonist," claims 11 and 12 have been amended to recite "mammal *as a* bolus," and claim 39 has been amended to delete the phrase "diabetes associated with a genetic syndrome." These amendments render the rejection under 35 U.S.C. § 112, second paragraph, moot. Withdrawal of this rejection is accordingly requested.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 1-22, 24-30, and 36-39 are rejected as failing to comply with the written description requirement. In particular, the Office applies the rejection to the terms "GLP-1 molecule having GLP-1 effect," as recited in claim 1, an exendin-4 analog or derivative, as recited in claim 22, and an insulin analog, as recited in claim 28.

The question of whether a claimed invention meets the written description requirement hinges on whether the specification demonstrates that the inventor has possession of the invention. Possession of a genus claim can be demonstrated by reduction to practice of a representative number of species of the claimed genus. As set

forth below, applicant has met this burden with respect to the amended claims. Each of the rejected terms is addressed below.

Rejection of GLP-1 related molecule with GLP-1 effect

Without assenting to this rejection, applicant has amended claim 1 and its dependent claims to recite a GLP-1 agonist. As explained above, the invention is based on the discovery that the therapeutic benefits of GLP-1 agonist activity continue after administration of the agonist has ceased. Because the specification demonstrates the effectiveness of a GLP-1 agonist in the claimed method, and because the specification provides many examples of GLP-1 agonists, one would understand the applicant to be in possession of the claimed invention. Withdrawal of this rejection is respectfully requested.

Rejection of exendin-4 analog or derivative

Claim 22 is rejected for reciting an exendin-4 analog or derivative. This term is rejected as lacking both a structural and a functional definition and on the grounds that only a few species are disclosed. Without assenting to this rejection, claim 22 has been amended to recite that the analog or derivative comprises an amino acid sequence at least 90% identical to exendin-4, or a fragment thereof, where the analog, derivative, or fragment increases endogenous insulin production. Based on these changes, claim 22 recites both a structure and a function of the exendin-4 derivative or analog. Further, the specification recites numerous examples of such exendin-4 analogs, for example, at page 16, line 17 through page 18, line 12.

Because claim 22, as amended, recites structural and functional limitations and because an adequate number of species are provided, this claim is free from the written description rejection. Withdrawal of this rejection is respectfully requested.

Rejection of insulin analog

Claim 28 is rejected for reciting the term "insulin analog." In making this rejection, the Office contends that this term fails to describe a structure or function. Without assenting to this rejection, applicants have amended the claims to recite that the insulin analog is "a recognized anti-diabetic drug."

Anti-diabetic insulin analog drugs are readily identified. As shown in Exhibit A, a search on the FDA website (http://www.accessdata.fda.gov/Scripts/cder/DrugsatFDA/) for drugs containing the word "insulin" yielded approximately 65 hits. Most of these hits correspond to forms of human, porcine, or beef insulin. The remaining hits are directed to insulin analogs, including insulin glulisine (Apidra™), insulin lispro (Humalog, etc.), insulin glargine (Lantus), insulin aspart (Novolog), and insulin detemir (Levemir). Thus, insulin analogs that are "recognized anti-diabetic drugs" is a genus that is readily ascertainable by one skilled in the art. Withdrawal of the written description rejection on this basis is respectfully requested.

Rejection under 35 U.S.C. § 103(a)

Claims 1-22, 24-30, and 36-39 are rejected as being obvious over Larsen in view of Roach. In making this rejection, the Office cites Larsen as disclosing Compound 1. Roach is cited as disclosing Lispro (Lys(B28)Pro(B29) human insulin). The Office takes the position that administering combination of two known equivalents (in this case, two drugs for treating diabetes) is obvious. The Office further states that the dependent claims recite only routine optimization and thus fall within the purview of the ordinary skilled artisan. Applicant respectfully disagrees.

Claim 1 requires that there not be continuous presence of the GLP-1 agonist, and claims 2-9 require dose reductions and lengths of time in which there is a dose reduction (e.g., a "drug holiday"). These claims are based on applicant's discovery that the therapeutic benefits of GLP-1 agonist administration continue for a significant period of time period after administration of the agonist ends.

For a combination of references to render a claim obvious, the references must teach every claim limitation. Larsen fails to teach administration of a GLP-1 agonist such that the agonist is not continuously present, as recited in claim 1 and its dependent claims. Roach, which discloses administration of Humalog Mix25, fails to overcome the deficiency of Larsen. In particular, Roach does not disclose GLP-1 agonist administration at all, much less administration of a GLP-1 agonist (or any other agent) in a non-continuous manner.

Accordingly, no combination of Larsen and Roach teach the non-continuous administration recited in claim 1. And these references certainly do not teach the specific parameters for administration recited in claims 2-9 as well. Because these references fail to teach every claim limitation, Larsen and Roach cannot render the pending claims as being obvious. Withdrawal of the rejection under 35 U.S.C. § 103(a) is respectfully requested.

Obviousness-type double patenting rejection

Claims 1-22, 24-30, and 36-39 are provisionally rejected as being obvious over claims 1-8 of the '148 application. Applicant respectfully traverses this rejection. As explained above, the claims of the present application require that the GLP-1 agonist not be continuously present. The claims of the '148 application do not teach or suggest this limitation, and therefore cannot render the present claims obvious.

Should the Office maintain this rejection, notwithstanding the failure of the '148 claims to render the present claims obvious, applicant requests that this rejection be held in abeyance. Once the other rejections have been addressed, it would be proper to allow the present claims to issue as the present application is the earlier of the two filed applications (M.P.E.P. § 804(I)(B)(1)).

CONCLUSION

Applicant submits that the claims are in condition for allowance, and such action is respectfully requested. If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: March 18, 2010

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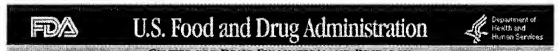

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APIDRA SOLOSTAR	**INSULIN** GLULISINE RECOMBINANT
EXUBERA	**INSULIN** RECOMBINANT HUMAN
HUMALOG	**INSULIN** LISPRO RECOMBINANT
HUMALOG KWIKPEN	**INSULIN** LISPRO RECOMBINANT
HUMALOG MIX 50/50	INSULIN LISPRO PROTAMINE RECOMBINANT; **INSULIN** LISPRO RECOMBINANT
HUMALOG MIX 50/50 KWIKPEN	INSULIN LISPRO PROTAMINE RECOMBINANT; **INSULIN** LISPRO RECOMBINANT
HUMALOG MIX 75/25	INSULIN LISPRO PROTAMINE RECOMBINANT; **INSULIN** LISPRO RECOMBINANT
HUMALOG MIX 75/25 KWIKPEN	INSULIN LISPRO PROTAMINE RECOMBINANT; **INSULIN** LISPRO RECOMBINANT
HUMALOG PEN	**INSULIN** LISPRO RECOMBINANT
HUMULIN 50/50	INSULIN RECOMBINANT HUMAN; **INSULIN** SUSP ISOPHANE RECOMBINANT HUMAN
HUMULIN 70/30	INSULIN RECOMBINANT HUMAN; **INSULIN** SUSP ISOPHANE RECOMBINANT HUMAN
HUMULIN 70/30 PEN	INSULIN RECOMBINANT HUMAN; **INSULIN** SUSP ISOPHANE RECOMBINANT HUMAN
HUMULIN BR	**INSULIN** RECOMBINANT HUMAN
HUMULIN L	**INSULIN** ZINC SUSP RECOMBINANT HUMAN
HUMULIN N	**INSULIN** SUSP ISOPHANE RECOMBINANT HUMAN
HUMULIN R	**INSULIN** RECOMBINANT HUMAN

Exhibit A

HUMULIN R PEN	**INSULIN** RECOMBINANT HUMAN
HUMULIN U	**INSULIN** ZINC SUSP EXTENDED RECOMBINANT HUMAN
ILETIN I	**INSULIN** PORK
ILETIN II	**INSULIN** PURIFIED PORK
INSULATARD NPH HUMAN	**INSULIN** SUSP ISOPHANE SEMISYNTHETIC PURIFIED HUMAN
INSULIN	**INSULIN** PORK
INSULIN INSULATARD NPH NORDISK	**INSULIN** SUSP ISOPHANE PURIFIED PORK
INSULIN NORDISK MIXTARD (PORK)	**INSULIN** PURIFIED PORK, **INSULIN** SUSP ISOPHANE PURIFIED PORK
LANTUS	**INSULIN** GLARGINE RECOMBINANT
LENTARD	**INSULIN** ZINC SUSP PURIFIED BEEF/PORK
LENTE	**INSULIN** ZINC SUSP PURIFIED PORK
LENTE ILETIN II	**INSULIN** ZINC SUSP PURIFIED BEEF
LENTE ILETIN II (PORK)	**INSULIN** ZINC SUSP PURIFIED PORK
LENTE **INSULIN**	**INSULIN** ZINC SUSP BEEF
LEVEMIR	**INSULIN** DETEMIR
LEVEMIR	**INSULIN** DETEMIR RECOMBINANT
MIXTARD HUMAN 70/30	INSULIN RECOMBINANT PURIFIED HUMAN, **INSULIN** SUSP ISOPHANE SEMISYNTHETIC PURIFIED HUMAN
NOVOLIN 70/30	INSULIN RECOMBINANT HUMAN; **INSULIN** SUSP ISOPHANE RECOMBINANT HUMAN
NOVOLIN 70/30	INSULIN RECOMBINANT PURIFIED HUMAN **INSULIN** SUSP ISOPHANE SEMISYNTHETIC PURIFIED HUMAN
NOVOLIN L	**INSULIN** ZINC SUSP RECOMBINANT HUMAN
NOVOLIN L	**INSULIN** ZINC SUSP SEMISYNTHETIC PURIFIED HUMAN
NOVOLIN N	**INSULIN** SUSP ISOPHANE RECOMBINANT HUMAN
NOVOLIN N	**INSULIN** SUSP ISOPHANE SEMISYNTHETIC PURIFIED HUMAN
NOVOLIN R	**INSULIN** RECOMBINANT HUMAN
NOVOLIN R	**INSULIN** RECOMBINANT PURIFIED HUMAN
NOVOLOG	**INSULIN** ASPART RECOMBINANT
NOVOLOG MIX 50/50	INSULIN ASPART PROTAMINE RECOMBINANT; **INSULIN** ASPART RECOMBINANT
NOVOLOG MIX 70/30	INSULIN ASPART PROTAMINE RECOMBINANT; **INSULIN** ASPART RECOMBINANT
NPH ILETIN I (BEEF-PORK)	**INSULIN** SUSP ISOPHANE BEEF/PORK

Exhibit A

NPH ILETIN II	**INSULIN** SUSP ISOPHANE PURIFIED BEEF
NPH ILETIN II (PORK)	**INSULIN** SUSP ISOPHANE PURIFIED PORK
NPH **INSULIN**	**INSULIN** SUSP ISOPHANE BEEF
NPH PURIFIED PORK ISOPHANE **INSULIN**	**INSULIN** SUSP ISOPHANE PURIFIED PORK
PROTAMINE ZINC & ILETIN I (BEEF-PORK)	**INSULIN** SUSP PROTAMINE ZINC BEEF/PORK
PROTAMINE ZINC AND ILETIN II	**INSULIN** SUSP PROTAMINE ZINC PURIFIED BEEF
PROTAMINE ZINC AND ILETIN II (PORK)	**INSULIN** SUSP PROTAMINE ZINC PURIFIED PORK
PROTAMINE ZINC **INSULIN**	**INSULIN** SUSP PROTAMINE ZINC PURIFIED BEEF
REGULAR ILETIN II	**INSULIN** PURIFIED BEEF
REGULAR ILETIN II (PORK)	**INSULIN** PURIFIED PORK
REGULAR **INSULIN**	**INSULIN** PORK
REGULAR PURIFIED PORK **INSULIN**	**INSULIN** PURIFIED PORK
SEMILENTE	**INSULIN** ZINC SUSP PROMPT PURIFIED PORK
SEMILENTE **INSULIN**	**INSULIN** ZINC SUSP PROMPT BEEF
ULTRALENTE	**INSULIN** ZINC SUSP EXTENDED PURIFIED BEEF
ULTRALENTE **INSULIN**	**INSULIN** ZINC SUSP EXTENDED BEEF
VELOSULIN	**INSULIN** PURIFIED PORK
VELOSULIN BR	**INSULIN** RECOMBINANT HUMAN
VELOSULIN BR HUMAN	**INSULIN** RECOMBINANT PURIFIED HUMAN

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Exhibit A